REMARKS/ARGUMENTS

Claims 1-20 are currently pending in the application. Claims 18 and 19 have been amended by this response. It is respectfully submitted that the following remarks present no new issues or new matter and place this case in condition for allowance. Reconsideration of the application in view of the following remarks is respectfully requested.

I. Rejection of Claims 1-17 under 35 U.S.C. § 103(a)

Claims 1-17 are rejected under 35 U.S.C. § 103(a) as being obvious over U.S. 4,929,605 to Domet et al. ("Domet") in combination with U.S. 4,176,175 to Maekawa et al. ("Maekawa"). The rejection is respectfully traversed.

Domet discloses in examples 1 and 2 (columns 5 and 6), pharmaceutical compositions containing *terfenadine* and calcium carbonate. These examples teach compositions containing *only terfenadine*. Domet does not provide any examples that teach the use of fexofenadine. In addition, the examples of Domet disclose that *calcium carbonate* is an essential component of the composition. Calcium carbonate is an ingredient which Applicants' claims exclude. The Examiner states "fexofenadine and terfenadine...are quite similar in structure differing "only" by a substituent (i.e. methyl group as opposed to a carboxyl group)." However, there is a significant chemical difference between methyl and carbonyl. Methyl is a non-reactive and non-polar moiety, while carbonyl is highly polar and very reactive. The structural difference results in a dramatic difference in the pharmacological properties of the molecules. Terfenadine is no longer marketed having been discontinued because of potentially lethal cardiac side effects, while fexofenadine is presently being commercially marketed. Thus, fexofenadine is *not* equivalent to terfenadine, either structurally or functionally. Thus, Domet fails to disclose Applicants' claimed composition or method of preparation.

Maekawa discloses in column 4, lines 17-22 "...syrups used in the subcoating and smoothing steps in accordance with the present invention may contain gelatin, which works to effect the extension of disintegration time of the sugar-coated solid dosage forms, alone or in combination with a gum, as in the prior art." It is noted that in Examples 1-7, the coating syrups prepared by Maekawa contain *gum arabic* in addition to sugar and low-substituted hydroxypropyl cellulose. One skilled in the art would conclude from these teachings that gum arabic is an *essential* component in the coating composition in order to achieve improved disintegration. Thus, Maekawa fails to disclose Applicants' claimed composition or method of preparation.

Further, the motivation or suggestion to combine references in the manner suggested by the Examiner must come from the applied references. There is no disclosure, direction, or motivation in either Domet or Maekawa to suggest the combination suggested by the Examiner. Domet states in column 1, lines 30-33 "[a] novel pharmaceutical composition is now provided which allows efficient and immediate absorption bioavailability of these compounds after oral administration." One skilled in the art would conclude that Domet has provided a successful, working formulation, and there would be no motivation to combine any part of Maekawa's composition to Domet's composition.

Assuming arguendo, even if motivation to combine the references in the manner suggested by the Examiner did exist in the applied references, the resultant combination still would not disclose Applicants' claimed invention. One skilled it the art would conclude from the teachings of Domet that *calcium carbonate is an essential component* that must be included in order to achieve a bioavailable composition. One skilled in the art would also conclude from the teachings of Maekawa that *gum arabic* is an essential component that must be included in order to achieve tablets with improved disintegration leading to improved bioavailability. Applicants' invention as claimed does not include calcium carbonate or gum arabic, and through the use of "consisting essentially of" language in Claim 1, Applicants have excluded their use that would materially affect the basic and novel characteristics of Applicants' invention as claimed. For the reasons set forth hereinabove, the Examiner has not established a *prima facie* case for obviousness under 35 U.S.C. § 103 and withdrawal of this ground of rejection is respectfully requested.

II. Rejection of Claims 18-20 under 35 U.S.C. § 103(a)

Claims 18-20 are rejected under 35 U.S.C. § 103(a) as obvious over Domet in combination with U.S. 6,380,381 to Obara et al. ("Obara"). This rejection is respectfully traversed.

The Examiner states the difference between Applicants' method and the method disclosed by Domet is that Applicants use low-substituted hydroxypropyl cellulose in their composition. In Examples 1 and 2 (columns 5 and 6), Domet discloses a method for the preparation of a pharmaceutical composition containing terfenadine. Table 1 shows a comparison of Domet's method of preparing a pharmaceutical composition with the method claimed by Applicants in Claim 18.

Table 1: Methods of Preparing a Pharmaceutical Composition

Domet's Method	Applicants' Method of Claim 18
(a) mixing *terfenadine*, microcrystalline cellulose, *calcium carbonate*, and pregelatinized starch	(a) mixing fexofenadine, lactose, and low-substituted hydroxypropyl cellulose to form a premix
(b) adding polysorbate 80 in water to the premix formed in Step (a) to form a wet granulation	(b) adding a solvent to the premix formed in Step (a) to form a wet granulation
(c) passing the granules through a 10 mesh screen	
(d) drying the granules	(c) drying the wet granulation to form dried granules
(e) mixing the granules with pregelatinzed corn starch, starch glycolate sodium, magnesium stearate	(d) mixing at least one excipient with the dried granules to form a pharmaceutical composition

Domet fails to disclose Applicants' method for preparing a pharmaceutical composition containing fexofenadine. Domet also fails to disclose Applicants' claimed method using low-substituted hydroxypropyl cellulose. Further, Domet fails to disclose Applicants' claimed method which excludes calcium carbonate which is essential to Domet's composition. Through the use of "consisting essentially of" language in Claims 18 and 19, Applicants have excluded the use of such ingredients that would materially affect the basic and novel characteristics Applicants' invention as claimed.

The Examiner states Obara discloses that low-substituted hydroxypropyl cellulose exhibits good granulation characteristics and tablet properties.

Obara discusses in column 1, lines 39-56:

> In the case of low-substituted hydroxypropyl cellulose, its degree of substitution and particle size have been considered to be important factors affecting its binding properties. However, it has frequently been recognized that, even if these factors are controlled, the disintegration of tablets may be delayed as a result of abnormally advanced granulation, or the hardness of tablets may be reduced as a result of unsatisfactory granulation characteristics.
>
> In order to overcome these disadvantages of the prior art, the present inventors made intensive investigations and have now found that the degree of polymerization or molecular weight of low-substituted hydroxypropyl cellulose affects its binding properties in wet granulation. The present invention has been completed on the basis of this finding.
>
> That is, the present invention provides low-substituted hydroxypropyl cellulose having a hydroxypropoxyl content in the range of 5.0 to 16.0% by weight and an apparent average degree of polymerization in the range of 350 to 700.

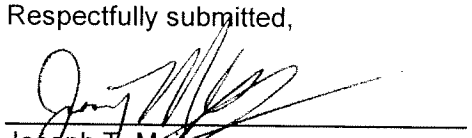
However, Obara discloses the use of low-substituted hydroxypropyl cellulose having a hydroxypropyl content in the range of 5.0% to 16.0% by weight *and* an apparent average degree

of polymerization in the range of 350 to 700 provides superior granulation characteristics and tablet properties over low-substituted hydroxypropyl cellulose of the prior art. Obara's results show low-substituted hydroxypropyl cellulose having an apparent average degree of polymerization from 350 to 700 affords good granulation characteristics while low-substituted hydroxypropyl cellulose having an apparent average degree of polymerization *outside* of this range affords *poor* granulation characteristics, tablet hardness, and disintegration time (Table 1, Columns 5 and 6). Clearly, it is the *apparent average degree of polymerization* of low-substituted hydroxypropyl cellulose that is essential to obtaining tablets exhibiting favorable disintegration, not the use of low-substituted hydroxypropyl cellulose itself.

Further, the motivation or suggestion to combine references in the manner suggested by the Examiner must come from the applied references. There is no disclosure, direction, or motivation in the art for one skilled to combine Obara with Domet as suggested by the Examiner. Domet states in column 1, lines 30-33 "[a] novel pharmaceutical composition is now provided which allows efficient and immediate absorption bioavailability of these compounds after oral administration." Applicants do not find any teachings in Domet that would suggest any problem or weakness in Domet's granulation. One skilled in the art would conclude that Domet has provided a successful, working formulation, and there would be no motivation to combine any part of Obara to Domet's composition. If the Examiner maintains this rejection, the Examiner is respectfully requested, in the next Office Action, to point specifically to the source of such motivation within Domet or Obara. For the reasons set forth hereinabove, the Examiner has not established a *prima facie* case for obviousness under 35 U.S.C. § 103 and withdrawal of this ground of rejection is respectfully requested.

In view of the above, it is respectfully submitted that all of the claims are in condition for allowance, and a Notice of Allowance is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,



Joseph T. Majka
Attorney for Applicants
Reg. No. 30,570

Novartis
Corporate Intellectual Property
One Health Plaza, Building 104
East Hanover, NJ 07936-1080
(609) 627-8508
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